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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/760,574	01/16/2001	Jean-Christophe Francis Audonnet	454313.3154.1	2896

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FROMMER LAWRENCE & HAUG
745 FIFTH AVENUE- 10TH FL.
NEW YORK, NY 10151

EXAMINER	
ANGELL, JON E	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/760,574	AUDONNET ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *84-220* is/are pending in the application.

4a) Of the above claim(s) *119-220* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *84-118* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5-21-03* 4 16
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This Action is in response to the communication filed on 12/4/03. Claims 84-220 are pending in the application and are addressed herein.

2. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Election/Restrictions

3. Claims 119-220 have previously been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim, for the reasons of record. Applicant timely traversed the restriction (election) requirement in a previous communication.

4. This application contains claim drawn to an invention nonelected with traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 103

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claims 84, 85 and 118 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Cox et al. (J. Virol. Vol. 67, pages 5664-5667; IDS reference AT) in view of in view of in view of Klavinskis et al. (J. Immunol. Vol. 162, No. 1, pages 254-262; January 1, 1999), for the reasons of record.

7. Claims 84-91 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Cox et al. (J. Virol. Vol. 67, pages 5664-5667; IDS reference AT) in view of Klavinskis et al. (J. Immunol. Vol. 162, No. 1, pages 254-262; January 1, 1999) and further in view of Xiang et al. (Immunity 1995, 2:129-135), and Baker et al. (US Patent 5,106,733; 1992), for the reasons of record.

8. Claims 84, 92, 94, 100 and 104 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Cox et al. (J. Virol. Vol. 67, pages 5664-5667; IDS reference AT) in view of in view of Klavinskis et al. (J. Immunol. Vol. 162, No. 1, pages 254-262; January 1, 1999) and further in view of Li (WO 96/40945), for the reasons of record.

9. Claims 84, 93, and 104 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Cox et al. (J. Virol. Vol. 67: 5664-5667; 1993; IDS # AT) in view of Klavinskis et al. (J. Immunol. Vol. 162, No. 1, pages 254-262; January 1, 1999) and further in view of Choi et al. (Virology 1998, 250:230-240), for the reasons of record.

10. Claims 84-95, 100-111 and 118 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Cox et al. (J. Virol. Vol. 67: 5664-5667; 1993; IDS # AT) in view of Klavinskis et al. (J. Immunol. Vol. 162, No. 1, pages 254-262; January 1, 1999) and further in view of Xiang et al. (Immunity 1995, 2:129-135), Baker et al. (US Patent 5,106,733; 1992), Li (WO 96/40945), and Choi et al. (Virology 1998, 250:230-240), for the reasons of record.

Double Patenting

11. Claims 84-118 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, 5 and 16-19 of

copending Application No. 09/766,442. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to a BRSV vaccine. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

12. Claims 84, 85, 96, 112, and 116-118 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 5-8 of U.S. Patent No. 6,376,473 B1 (Audonnet) in view of in view of Klavinskis et al. (J. Immunol. Vol. 162, No. 1, pages 254-262; January 1, 1999).

13. Claims 84-91 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 5-8 of U.S. Patent No. 6,376,473 B1 (Audonnet) in view of Klavinskis et al. (J. Immunol. Vol. 162, No. 1, pages 254-262; January 1, 1999) and further in view of Xiang et al. (Immunity 1995, 2:129-135), and Baker et al. (US Patent 5,106,733; 1992).

14. Claims 84, 92, 94, 95, 100 and 108 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 5-8 of U.S. Patent No. 6,376,473 B1 (Audonnet) in view of Klavinskis et al. (J. Immunol. Vol. 162, No. 1, pages 254-262; January 1, 1999) and further in view of Li (WO 96/40945).

15. Claims 84, 93, 97, 98 and 104 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 5-8 of U.S. Patent No.

6,376,473 B1 (Audonnet) in view of Klavinskis et al. (J. Immunol. Vol. 162, No. 1, pages 254-262; January 1, 1999) and further in view of Choi et al. (Virology 1998, 250:230-240).

16. Claims 84-118 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 5-8 of U.S. Patent No. 6,376,473 B1 (Audonnet) in view of Klavinskis et al. (J. Immunol. Vol. 162, No. 1, pages 254-262; January 1, 1999) and further in view of Xiang et al. (Immunity 1995, 2:129-135), Baker et al. (US Patent 5,106,733; 1992), Li (WO 96/40945), and Choi et al. (Virology 1998, 250:230-240).

Response to Arguments

17. Applicant's arguments filed 12/4/03 have been fully considered but they are not persuasive.

18. Applicants argue that there is no suggestion or motivation to modify the reference teachings and, additionally, that there would be no expectation of success. Specifically applicants point out that many of the references cited in the prior action involved experiments in mice. Applicants refer to a prior art teaching that DNA vaccine experiments successfully completed in mice do not always work in larger species, and, as such, one of ordinary skill in could not extrapolate vaccine data for smaller animals such as mice to larger animals such as bovines. Furthermore, applicants contend that there is no teaching or suggestion present in any of the references which would encourage one of skill in the art to combine the references in order to arrive at the present invention. Applicants assert that Cox et al., Klavinskis et al., Xiang et al.,

Baker et al., Li and Choi et al., are primarily concerned with mice. There is no teaching or suggestion that such findings may be extrapolated to larger animals, including bovines. Furthermore, applicants believe that the references are so dissimilar that one would not be motivated to combine them.

19. In response, it is reiterated that the claims are drawn to a vaccine against a bovine pathogen wherein the vaccine comprises at least one plasmid encoding an immunogen of the bovine pathogen and other compounds which would improve the efficacy of the vaccine, such as a cationic lipid (such as DMRIE/DOPE) (e.g., see claim 84); bovine GM-CSF, DMRIE and/or DOPE. Additionally, claims also encompass making structural modifications to the immunogen, such as deleting the transmembrane portion, adding a heterologous tPA signal sequence, and/or adding intron II of the rabbit beta-globin gene.

20. As indicated in the previous Office Actions, the plasmid DNA to a bovine pathogen (BHV) was known in the art. Additionally, all of the modifications encompassed by the claims are art-recognized modifications that one of ordinary skill in the art would find obvious to make to a DNA vaccine in order to enhance the hosts immune response to the vaccine thus increasing the efficacy of the vaccine.

21. With respect to applicants arguments that most of the references cited involve experiments performed in mice, and the prior art indicates that results found in mice cannot be extrapolated to larger animals, it is respectfully pointed out that Schultz is commenting on ***DNA vaccines***. Schultz does indeed indicate that DNA vaccines that are shown to work in mice cannot always be extrapolated to larger animals. However, in the instant case, the DNA vaccine has already been found to work in bovines. Cox clearly teaches a DNA vaccine that is effective

in bovines. Therefore, the only questions are, would the modifications to the bovine DNA vaccine be obvious to one of ordinary skill in the art, and when combined with the bovine DNA vaccine, would there be an expectation of success?

With respect to the teachings of Schultz, it is clear that not all DNA vaccines that work in mice will work in larger animals. Cox overcomes this problem by showing a DNA plasmid that works in mice and bovines. Furthermore, Schultz is silent with respect to the effect of the claimed modifications to the DNA vaccine in larger animals. That is, Schultz does not indicate that the claimed modifications would not extrapolate to larger animals. It is pointed out that many of the modifications to the bovine vaccine are simply the addition of well-known adjuvants. As indicated in the prior art (See: Bonnem, WO 94/01133, of record):

> "One problem that frequently is encountered in the course of active immunization is that the antigens used in the vaccine are not sufficiently immunogenic to raise an antibody titer to sufficient levels to provide protection against subsequent challenge, or to maintain the potential for mounting these levels over extended time periods. Another problem is that the vaccine may be deficient in inducing cell-mediated immunity which is a primary immune defense against bacterial and viral infection. Still another problem is that an individual patient might be immunosuppressed. To obtain a stronger humoral and/or cellular response, it is common to administer a vaccine in a formulation containing an adjuvant. **An adjuvant is a substance that enhances, NONSPECIFICALLY, the immune response to an antigen**, or which causes an individual to respond to an antigen who would otherwise without the adjuvant not respond to the antigen. An adjuvant is usually administered with an antigen, but may also be given before or after antigen administration." (See pages 1-2 of Bonnem, emphasis added)

Therefore, it is clear that adjuvants are substances which NONSPECIFICALLY enhance the immune response to an antigen. Since the prior art indicates the adjuvants nonspecifically enhance the immune response to antigens, one of ordinary skill in the art would have been motivated to add adjuvants to the bovine vaccine. Furthermore, considering that the prior art teaches that adjuvants nonspecifically enhance immune responses, and considering that there is

no evidence presented that the adjuvants would not enhance the immune response of larger animals, including bovines, one of ordinary skill in the art would also have a reasonable expectation of success that adding an adjuvant to a bovine plasmid vaccine would enhance the bovine's immune response to the vaccine.

With respect to the modifications of the immunogen encompassed by the claims, such as deleting the transmembrane domain, adding a tPA signal sequence and adding intron II of the rabbit beta-globin gene, it is respectfully pointed out that the prior art (Li) teaches, (as previously indicated) that the deletion of the transmembrane region of an immunogen results in a secreted form of the immunogen (see p. 5, line 35 through p. 6, line 1) resulting in an increase in the efficacy of the vaccine (see p. 27, lines 2-21). In fact, Li indicates that only the vaccine comprising the deletion of the transmembrane of the immunogen results in complete protection (see p. 27, lines 14-21). Additionally, Li teaches modifying the vaccine such that it comprises the nucleotide sequence of the rabbit beta-globin intron 11 in order to prevent aberrant mRNA splicing, thus stabilizing the mRNA and enhancing the immunoprotective ability of the vaccine (see p. 6, lines 26-32). Therefore, it is would have been obvious to one of ordinary skill in the art to modify the immunogen such that it comprised any of these modifications in order to enhance the efficacy of the vaccine. Since the prior art indicates that these modifications enhance the efficacy of a vaccine, one of ordinary skill in the art would be motivated to make these modifications to other vaccines, including the bovine DNA vaccine. Furthermore, since there is no evidence presented and since there is no indication in the prior art that these modifications would not work in bovine DNA vaccines, one of ordinary skill in the art would have a reasonable

expectation of success as well. Therefore, the rejection of claims under 35 USC 103 are not withdrawn.

With respect to the provisional double patenting rejection, Applicants indicate that the rejection should be withdrawn from this application an applied to the '442 application after allowance of this application.

In response, it is respectfully pointed out that it is proper to maintain a provisional double patenting rejection in all applications until one application is allowed, at which time the double patenting rejection in all other applications is no longer provisional. Therefore, the provisional double patenting rejection is not withdrawn at this time, but should this application become allowed, the provisional rejection will be withdrawn.

Regarding the remaining rejections, Applicants contend that there is no motivation to combine any of the documents, and also argue that a combination of such documents does not cure the deficiencies of Audonnet or render obvious the present invention.

In response, for the reasons indicated previously and herein, one of ordinary skill in the art would have had motivation to combine the references, and the combination of documents does cure the deficiencies of Audonnet.

Conclusion

22. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (571) 272-0756. The examiner can normally be reached on M-F (8:00-5:30) with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

J. Eric Angell, Ph.D.
Art Unit 1635

PRIMARY EXAMINER